

Att'y Dkt. No. US-1310

U.S. App. No: 09/926,299

IN THE CLAIMS:

Kindly rewrite the claims as follows, in accordance with 37 C.F.R. § 1.121:

1. (currently amended) An isolated strain of *Methylophilus methylotrophus* having ~~L-amino acidlysine~~-producing ability, wherein ~~L-amino acid biosynthetic enzyme~~ dihydrodipicolinate synthase activity is enhanced as compared to a wild-type *Methylophilus methylotrophus* strain, and wherein said dihydrodipicolinate synthase is selected from the group consisting of:

a) a protein encoded by the DNA sequence depicted in a nucleotide sequence comprising nucleotide numbers 1268 to 2155 of SEQ ID NO:9; and

b) a protein encoded by a DNA sequence which hybridizes to the DNA sequence depicted in a nucleotide sequence comprising nucleotide numbers 1268 to 2155 of SEQ ID NO:9 under stringent conditions, wherein said conditions comprise washing at 60°C in a salt solution of 1xSSC and 0.1%SDS.

2. (currently amended) The isolated strain according to claim 1, wherein the L-amino acid is ~~selected from the group consisting of~~ L-lysine, L-valine, L-leucine, L-isoleucine, and L-threonine.

3. (cancelled)

4. (cancelled)

5. (currently amended) ~~The isolated strain according to claim 1,~~ An isolated strain of *Methylophilus methylotrophus* having L-lysine-producing ability, wherein dihydrodipicolinate synthase activity and aspartokinase activity are enhanced as compared to a wild-type *Methylophilus methylotrophus* strain, and wherein said isolated strain has L-lysine-producing ability and wherein said dihydrodipicolinate synthase is selected from the group consisting of:

a) a protein encoded by the DNA sequence depicted in a nucleotide sequence

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comprising nucleotide numbers 1268 to 2155 of SEQ ID NO:9; and

b) a protein encoded by a DNA sequence which hybridizes to the DNA sequence depicted in a nucleotide sequence comprising nucleotide numbers 1268 to 2155 of SEQ ID NO:9 under stringent conditions, wherein said conditions comprise washing at 60°C in a salt solution of 1xSSC and 0.1%SDS,

and wherein said aspartokinase is selected from the group consisting of:

a) a protein encoded by the DNA sequence depicted in a nucleotide sequence comprising a nucleotide numbers 510 to 1736 of SEQ ID NO:5;

b) a protein encoded by a DNA sequence which hybridizes to the DNA sequence depicted in a nucleotide sequence comprising nucleotide numbers 510 to 1736 of SEQ ID NO:5 under stringent conditions, wherein said conditions comprise washing at 60°C in a salt solution of 1xSSC and 0.1%SDS.

6. (cancelled)

7. (currently amended) ~~The isolated strain according to claim 1, An isolated strain of *Methylophilus methylotrophus* having L-amino acid-producing ability, wherein aspartokinase activity is enhanced as compared to wild-type *Methylophilus methylotrophus* strain, and wherein said isolated strain has L-lysine-producing ability and wherein said aspartokinase is selected from the group consisting of:~~

a) a protein encoded by the DNA sequence depicted in a nucleotide sequence comprising a nucleotide numbers 510 to 1736 of SEQ ID NO:5;

b) a protein encoded by a DNA sequence which hybridizes to the DNA sequence depicted in a nucleotide sequence comprising nucleotide numbers 510 to 1736 of SEQ ID NO:5 under stringent conditions, wherein said conditions comprise washing at 60°C in a salt solution of 1xSSC and 0.1%SDS.

8. (previously presented) The isolated strain according to claim 5, wherein an activity or activities of one, two, or three of enzymes selected from the group consisting of aspartic acid semialdehyde dehydrogenase, dihydrolipicolinate reductase and diaminopimelate decarboxylase is/are enhanced as compared to a wild-type *Methylophilus methylotrophus*

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strain.

9. (previously presented) The isolated strain according to claim 5, wherein the dihydrodipicolinate synthase activity and the aspartokinase activity are enhanced as compared to a wild-type *Methylophilus methylotrophus* strain by introduction into cells of a DNA coding for dihydrodipicolinate synthase that does not suffer from feedback inhibition by L-lysine and a DNA coding for aspartokinase that does not suffer from feedback inhibition by L-lysine.

10. (currently amended) The isolated strain according to claim 17, wherein activities of ~~aspartokinase~~, homoserine dehydrogenase, homoserine kinase and threonine synthase are enhanced as compared to wild-type *Methylophilus methylotrophus* strain, and wherein said isolated strain has L-threonine-producing ability.

11. (cancelled)

12. (currently amended) A method for producing an ~~L-amino acid~~lysine, which comprises culturing said strain as defined in claim 1 in a medium, accumulating said ~~L-amino acid~~lysine in said medium, and collecting the ~~L-amino acid~~lysine from said medium.

13. (original) The method according to claim 12, wherein the medium contains methanol as a main carbon source.

14. (withdrawn) A method for producing bacterial cells of a *Methylophilus* bacterium with an increased content of an L-amino acid, which comprises culturing a *Methylophilus* bacterium as defined in claim 1 in a medium ~~to produce and accumulate an L-amino acid in bacterial cells of the bacterium.~~

15. (withdrawn) A method for producing bacterial cells of the *Methylophilus* bacterium according to claim 14, wherein the L-amino acid is L-lysine, ~~L-valine, L-isoleucine or L-~~

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threonine.

16. (withdrawn) A DNA which codes for a protein defined in the following (A) or (B):

- (A) a protein which has the amino acid sequence of SEQ ID NO: 6, or
- (B) a protein which has an amino acid sequences of SEQ ID NO:6 including substitution, deletion, insertion, addition, or inversion of one or several amino acids, and has aspartokinase activity.

17. (withdrawn) The DNA according to claim 16, which is a DNA defined in the following (a) or (b):

- (a) a DNA which has a nucleotide sequence comprising the nucleotide sequence of the nucleotide numbers 510 to 1736 of SEQ ID NO:5; or
- (b) a DNA which is hybridizable with a probe having the nucleotide sequence of the nucleotide numbers 510 to 1736 of SEQ ID NO:5 or a part thereof under a stringent condition, and codes for a protein having aspartokinase activity.

18. (withdrawn) The DNA which codes for a protein defined in the following (C) or (D):

- (C) a protein which has the amino acid sequence of SEQ ID NO: 8, or
- (D) a protein which has an amino acid sequences of SEQ ID NO:8 including substitution, deletion, insertion, addition, or inversion of one or several amino acids, and has aspartic acid semialdehyde dehydrogenase activity.

19. (withdrawn) The DNA according to claim 18, which is a DNA defined in the following (c) or (d):

- (c) a DNA which has a nucleotide sequence comprising the nucleotide sequence of the nucleotide numbers 98 to 1207 of SEQ ID NO:7; or
- (d) a DNA which is hybridizable with a probe having the nucleotide sequence of the nucleotide numbers 98 to 1207 of SEQ ID NO:7 or a part thereof under a stringent condition, and codes for a protein having aspartic acid semialdehyde dehydrogenase activity.

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20. (withdrawn) The DNA which codes for a protein defined in the following (E) or (F):

(E) a protein which has the amino acid sequence of SEQ ID NO:10, or

(F) a protein which has an amino acid sequences of SEQ ID NO:10 including substitution, deletion, insertion, addition, or inversion of one or several amino acids, and has dihydrodipicolinate synthase activity.

21. (withdrawn) The DNA according to claim 20, which is a DNA defined in the following (e) or (f):

(e) a DNA which has a nucleotide sequence comprising the nucleotide sequence of the nucleotide numbers 1268 to 2155 of SEQ ID NO:9; or

(f) a DNA which is hybridizable with a probe having the nucleotide sequence of the nucleotide numbers 1268 to 2155 of SEQ ID NO:9 or a part thereof under a stringent condition, and codes for a protein having dihydrodipicolinate synthase activity.

22. (withdrawn) The DNA which codes for a protein defined in the following (G) or (H):

(G) a protein which has the amino acid sequence of SEQ ID NO:12, or

(H) a protein which has an amino acid sequences of SEQ ID NO:12 including substitution, deletion, insertion, addition, or inversion of one or several amino acids, and has dihydrodipicolinate reductase activity.

23. (withdrawn) The DNA according to claim 22, which is a DNA defined in the following (g) or (h):

(g) a DNA which has a nucleotide sequence comprising the nucleotide sequence of the nucleotide numbers 2080 to 2883 of SEQ ID NO:11 or

(h) a DNA which is hybridizable with a probe having the nucleotide sequence of the nucleotide numbers 2080 to 2883 of SEQ ID NO:11 or a part thereof under a stringent condition, and codes for a protein having dihydrodipicolinate reductase activity.

24. (withdrawn) The DNA which codes for a protein defined in the following (I) or (J):

(I) a protein which has the amino acid sequence of SEQ ID NO:14, or

(J) a protein which has an amino acid sequences of SEQ ID NO:14 including

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substitution, deletion, insertion, addition, or inversion of one or several amino acids, and has diaminopimelate decarboxylase activity.

25. (withdrawn) The DNA according to claim 24, which is a DNA defined in the following (i) or (j):

- (i) a DNA which has a nucleotide sequence comprising the nucleotide sequence of the nucleotide numbers 751 to 1995 of SEQ ID NO:13; or
- (j) a DNA which is hybridizable with a probe having the nucleotide sequence of the nucleotide numbers 751 to 1995 of SEQ ID NO:13 or a part thereof under a stringent condition, and codes for a protein having diaminopimelate decarboxylase activity.

26. (currently amended) The isolated strain according to claim 61, wherein an activity or activities of one, two, or three of enzymes selected from the group consisting of aspartic acid semialdehyde dehydrogenase, dihydrodipicolinate reductase and diaminopimelate decarboxylase is/are enhanced as compared to a wild-type *Methylophilus methylotrophus* strain.

27. (currently amended) The isolated strain according to claim 72, wherein an activity or activities of one, two, or three of enzymes selected from the group consisting of aspartic acid semialdehyde dehydrogenase, dihydrodipicolinate reductase and diaminopimelate decarboxylase is/are enhanced as compared to a wild-type *Methylophilus methylotrophus* strain.

28. (new) A method for producing an L-lysine, which comprises culturing said strain as defined in claim 5 in a medium, accumulating said L-lysine in said medium, and collecting the L-lysine from said medium.

29. (new) The method according to claim 28, wherein the medium contains methanol as a main carbon source.

30. (new) A method for producing an L-amino acid, which comprises culturing said

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strain as defined in claim 7 in a medium, accumulating said L-amino acid in said medium, and collecting the L-amino acid from said medium.

31. (new) The method according to claim 30, wherein the medium contains methanol as a main carbon source.

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